

**IN THE CLAIMS**

1. (currently amended) A method for producing nonhuman mammalian embryos comprising the following steps:

(a) ~~evaluate and/or determining~~ the asynchrony of development (T) between two embryos of the same species and of the same age:

(i) ~~the wherein a first embryo being is produced by crossing at the time  $t_0$  a vasectomized male, preferably vasectomized, with a female, who has preferably received hormone treatment to increase ovulation, the said first embryo being at least cultured, and/or manipulated in vitro, or cultured and manipulated in vitro; and~~

(ii) ~~the a second embryo being produced by crossing at the time  $t_0$  a fertile male with a female who has preferably received hormone treatment in order to increase ovulation, said second embryo being normally fertilized and obtained by parthenogenetic activation, the evaluation and/or determination taking place at the latest on or before the day of uterine implantation of said second embryo; and~~

(b) transferring an embryo which is ~~at least cultured, and/or manipulated, -or -cultured and manipulated in vitro~~ into ~~the a~~ uterus of a recipient female who was crossed with a vasectomized male at ~~the time  $t = t_0 + T$~~

( $\pm 25\% T$ ) ~~+~~.

~~(c) optionally, allow said embryo transferred in step b) to become implanted and to develop in the uterus of said recipient female.~~

2. (currently amended) The method ~~as claimed in~~ claim 1, ~~characterized in that~~ wherein said first embryo is cultured, ~~and/or manipulated, or cultured and manipulated in vitro at the latest up to the day of implantation.~~

3. (currently amended) The method ~~as claimed in~~ of claims 1 ~~and 2~~, characterized in that wherein the ~~evaluation and/or said~~ determination is carried out at a stage of development chosen from ~~the~~ a 1 cell stage, 2 cell stage, 4 cell stage, 8 cell stage, 16 cell stage, morula stage and blastocyst stage.

4. (currently amended) The method ~~as claimed in~~ of claim 3, characterized in that ~~wherein the said~~ evaluation and/or determination is carried out at the blastocyst stage.

5. (currently amended) The method ~~as claimed in~~ of claims 1 ~~to 4~~, characterized in that wherein the ~~evaluation and/or said~~ determination of the asynchrony of development T is carried out by cell counting.

6. (currently amended) The method ~~as claimed in~~ of claims 1 ~~to 5~~, characterized in that wherein said asynchrony of development T is at least 15 hours.

7. (currently amended) The method ~~as claimed in~~ of claim 16, characterized in that wherein said asynchrony of development T is about 24 hours.

8. (currently amended) The method ~~as claimed in~~ of claims 1 ~~to 7~~, characterized in that wherein said embryo transferred in step b) is cultured under the same conditions as said first embryo.

9. (currently amended) The method ~~as claimed in~~ of claims 1 ~~to 8~~, characterized in that wherein said embryo transferred in step b) is at ~~the~~ a 1 cell stage.

10. (currently amended) The method ~~as claimed in~~ of claims 1 ~~to 8~~, characterized in that wherein said embryo transferred in step b) is at ~~the~~ a 2 cell stage.

11. (currently amended) The method ~~as claimed in~~ of claims 1 ~~to 8~~, characterized in that wherein said embryo transferred in step b) is at ~~the~~ a 4 cell stage.

12. (currently amended) The method ~~as claimed in of~~ claims 1 ~~to 11~~, ~~characterized in that~~wherein said transferred embryo develops into a fetus.

13. (currently amended) The method ~~as claimed in of~~ claim 12, ~~characterized in that~~wherein said fetus develops into a newborn.

14. (currently amended) The method ~~as claimed in of~~ claims 1 ~~to 13~~, ~~characterized in that~~wherein said embryo cultured, and/or manipulated, or cultured and manipulated in vitro is a transgenic embryo.

15. (currently amended) The method ~~as claimed in of~~ claims 1 ~~to 13~~, ~~characterized in that~~wherein said embryo cultured, and/or manipulated, or cultured and manipulated in vitro is a reconstituted embryo obtained by nuclear transfer.

16. (currently amended) The method ~~as claimed in of~~ claims 1 ~~to 13~~, ~~characterized in that~~wherein said embryo cultured, and/or manipulated, or cultured and manipulated in vitro is a reconstituted transgenic embryo obtained by nuclear transfer.

17. (currently amended) The method ~~as claimed in of~~ claims 1 ~~to 16~~, ~~characterized in that~~wherein said mammal is selected from the group consisting of rodents, lagomorphs, hoofed animals, equine animals and non-human primates, ~~except humans~~.

18. (currently amended) The method ~~as claimed in of~~ claim 17, ~~characterized in that~~ wherein said mammal is a rodent selected from the group consisting of mice, rats, hamsters, and guinea pigs.

19. (currently amended) The method ~~as claimed in of~~ claim 17, ~~characterized in that~~ wherein said hoofed animal is selected from the group consisting of bovines, ovines, caprines and porcines.

20. (currently amended) The method ~~as claimed in of~~ claim 17, ~~characterized in that~~ wherein said lagomorph is rabbit.

21. (currently amended) ~~An nonhuman embryo of a mammal, except humans, and/or fetus, newborn, adult mammal, or cells derived therefrom, produced by a the method comprising or including the method as claimed in one of claims 1 to 20.~~

22. (currently amended) ~~An nonhuman embryo of a transgenic mammal, except humans, and/or fetus, newborn, adult mammal, or cells derived therefrom, produced by a the method comprising or including the method as claimed in one of claims 1 to 20.~~

23. (currently amended) ~~An nonhuman embryo of a mammal, except humans, reconstituted in vitro obtained by nuclear transfer, and/or fetus, newborn, adult mammal, or cells derived therefrom, produced by a the method comprising or including the method as claimed in one of claims 1 to 20.~~

24. (currently amended) ~~A progeny of said nonhuman adult mammal as claimed in claims 21 to 23.~~

25. (currently amended) ~~An in vitro method for cloning the a nonhuman mammal by nuclear transfer wherein the method comprises a step of using a nonhuman mammalian embryo according to the method of claim 1. comprising or including a method as claimed in any one of claims 1 to 20.~~

26. (currently amended) ~~A method for producing rabbit embryos comprising the following steps:~~

~~(a) evaluate and/or determining the asynchrony of development (T) between two same age rabbit embryos of the same age.~~

~~- wherein the a first embryo being is produced by crossing at the time  $t_0$  a vasectomized male, preferably vasectomized, with a female who has preferably received hormone treatment to increase ovulation, said first embryo being at least cultured, and/or manipulated, or cultured and manipulated in vitro; and~~

- ~~the a~~ second embryo being ~~is~~ produced by crossing at ~~the~~ time  $t_0$ , a fertile male with a female ~~who has~~ preferably received hormone treatment in order to increase ovulation, the second embryo being normally fertilized and obtained by parthenogenetic activation; ~~the evaluation and/or~~ said determination taking place at ~~the latest~~ on or before the day of uterine implantation of said second embryo normally fertilized or obtained by parthenogenetic activation; and

(b) transferring a rabbit embryo which is cultured, ~~and/or~~ manipulated, or cultured and manipulated in vitro, no older than ~~the~~ blastocyst stage into ~~the a~~ uterus of a recipient female who was crossed with a vasectomized male at ~~the~~ time  $t = t_0 + T (+/- 25\% T)$ ;

~~(c) optionally, allow said embryo transferred in step b) to become implanted and to develop in the uterus of said recipient female.~~

27. (currently amended) The method ~~as claimed in~~ of claim 26, ~~characterized in that~~ wherein the ~~evaluation and/or the~~ said determination is carried out at a stage of development between days D1 and D7 *post coitum*.

28. (currently amended) The method ~~as claimed in~~ of claim 27, ~~characterized in that~~ wherein the ~~evaluation and/or~~ said determination is carried out on day D5 *post coitum*.

29. (currently amended) The method ~~as claimed in~~ of claims 26 to 28, ~~characterized in that~~ wherein said asynchrony of development T is ~~23 hours +/- 25%~~ about 17.25 to 28.75 hours.

30. (currently amended) The method ~~as claimed in~~ of claims 26 to 29, ~~characterized in that~~ wherein said embryo cultured, ~~and/or~~ manipulated, or cultured and manipulated in vitro is a transgenic embryo.

31. (currently amended) The method ~~as claimed in~~ of claims 26 to 29, ~~characterized in that~~ wherein said embryo cultured,

~~and/or manipulated, or cultured and manipulated~~ in vitro is a reconstituted embryo obtained by nuclear transfer.

32. (currently amended) The method ~~as claimed in~~ of claims 26 ~~to 29, characterized in that~~ wherein said embryo cultured, ~~and/or manipulated, or cultured and manipulated~~ in vitro is a reconstituted transgenic embryo obtained by nuclear transfer.

33. (currently amended) The method ~~as claimed in~~ of claims 26 ~~to 32, characterized in that~~ wherein said embryo transferred in step b) is at ~~the~~ a 1 cell stage.

34. (currently amended) A rabbit embryo ~~and/or~~ fetus, newborn, adult rabbit, or cells derived therefrom, produced by a ~~the~~ method ~~comprising or including the method as claimed in one of claims 26 to 33.~~

35. (currently amended) A transgenic rabbit embryo ~~and/or~~ fetus, newborn, adult rabbit or cells derived therefrom, produced by a ~~the~~ method ~~comprising or including the method as claimed in one of claims 26 to 33.~~

36. (currently amended) An in vitro reconstituted rabbit embryo obtained by nuclear transfer, ~~and/or~~ fetus, newborn, adult rabbit, or cells derived therefrom, produced by a ~~the~~ method ~~comprising or including the method as claimed in one of claims 26 to 33.~~

37. (currently amended) A progeny of said adult rabbit as claimed in claims 34 ~~to 36.~~

38. (currently amended) An in vitro method ~~for~~ of cloning ~~of~~ rabbits by nuclear transfer comprising ~~or including the method as claimed in any one of claims 26 to 33.~~

39. (currently amended) An in vitro method for cloning rabbits by nuclear transfer, said method comprising the steps of:

- a) inserting a rabbit donor cell or a rabbit donor cell nucleus into a rabbit enucleated oocyte under conditions which make it possible to obtain a reconstituted embryo;

b) activating the reconstituted embryo obtained in step a);

c) transferring said reconstituted embryo into a surrogate rabbit, such that the reconstituted embryo develops into a fetus, ~~and possibly into a~~ or newborn; ~~and is characterized in that~~ whereby the method comprises or includes a method as claimed in ~~any one of claims 26 to 33.~~

40. (currently amended) ~~The method as claimed in~~ of claim 39, ~~characterized in that~~ wherein the transfer of nucleus into ~~the~~ a recipient cytoplasm is carried out by fusion of the donor cell and of the recipient cytoplasm.

41. (currently amended) ~~The method as claimed in~~ of claim 39, ~~characterized in that~~ wherein the transfer of nucleus into ~~the~~ a recipient cytoplasm is carried out by microinjection of the donor nucleus into the recipient cytoplasm.

42. (currently amended) ~~The method as claimed in~~ of claim 39, ~~characterized in that~~ wherein said activating the reconstituted embryo ~~on phase during in vitro culture~~ is carried out by adding simultaneously, successively or spaced out over time, to ~~the~~ culture medium for said reconstituted embryo, at least one protein kinase inhibitor and at least one inhibitor of protein synthesis.

43. (currently amended) ~~An~~ in vitro method for cloning nonhuman mammals, ~~except humans,~~ comprising the steps of:

a) inserting a donor cell or a donor cell nucleus into an enucleated oocyte of a mammal of ~~the~~ a same species or of a species different from that of the donor cell under conditions which make it possible to obtain a reconstituted embryo;

b) activating the reconstituted embryo obtained in step a);

c) transferring said reconstituted embryo into a surrogate female mammal, such that the reconstituted embryo

develops into a fetus, ~~characterized in that~~whereby said activation is carried out by adding simultaneously, successively or spaced out over time, to ~~the~~ culture medium for said reconstituted embryo, at least one protein kinase inhibitor and at least one inhibitor of protein synthesis.

44. (currently amended) ~~The method as claimed in of~~ claim 43, ~~characterized in that~~wherein said mammal is selected from the group consisting of rabbits, rodents, in particular rats, mice, and from bovines, ovines, caprines, porcines, equines, and nonhuman primates, with the exception of humans.

45. (currently amended) ~~The method as claimed in of~~ claim 42 ~~to 44, characterized in that~~wherein said protein kinase inhibitor is 6-DMAP and said inhibitor of protein synthesis is cycloheximide (CHX).

46. (currently amended) ~~Method A~~ a method for producing a recombinant protein by a transgenic animal comprising the step of producing an nonhuman mammalian embryo of a nonhuman mammal as claimed in according to the method of claims 1 to 20.

47. (currently amended) A method for producing a recombinant protein by a transgenic rabbit comprising the step of producing a rabbit embryo according to the method of as claimed in claims 26 to 33.

48. (currently amended) ~~The~~ A method of studying human pathology wherein the method comprises a step of using a nonhuman mammalian embryo according to the method of claim 1, as a model. use of a transgenic animal capable of being obtained by the method as claimed in claims 1 to 20 or of a transgenic rabbit capable of being obtained by the method as claimed in claims 26 to 33 as a model for studying human pathologies.

49. (currently amended) A method of using a transgenic animal to produce recombinant proteins wherein the method comprises a step of using a nonhuman mammalian embryo according to the method of claim 1. The use of a transgenic animal capable



~~of being obtained by the method as claimed in claims 1 to 20 or of a transgenic rabbit capable of being obtained by the method as claimed in claims 26 to 33 for the production of recombinant proteins.~~

50. (currently amended) The method of use according to ~~of~~ claim 49, ~~characterized in that~~ wherein said recombinant protein is produced in ~~the~~ milk of the transgenic animal.

51. (new) The method of claim 1, wherein said embryo transferred in step b) is implanted and allowed to develop in the uterus of said recipient female.

52. (new) The method of claim 1, wherein said female has received hormone treatment to increase ovulation.

53. (new) The method of claim 26, wherein said embryo transferred in step b) is implanted and allowed to develop in the uterus of said recipient female.

54. (new) The method of claim 26, wherein said female has received hormone treatment in order to increase ovulation.

55. (new) The method of claim 26, wherein said asynchrony of development T is about 23 hours.

56. (new) The method of claim 43, wherein said protein kinase inhibitor is 6-DMAP and said inhibitor of protein synthesis is cycloheximide (CHX).